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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/541,094	03/31/2000	Peter H. St. George-Hyslop	1034/1F812-US2	4017

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EXAMINER
WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/541,094	Applicant(s) ST. GEORGE-HYSLOP ET AL.	
	Examiner Joseph Woitach	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,18-28,30 and 46-65* is/are pending in the application.

4a) Of the above claim(s) *1-6,18-28 and 30* is/are withdrawn from consideration.

5)☒ Claim(s) *46-50* is/are allowed.

6)☒ Claim(s) *51,54,55,59-62 and 65* is/are rejected.

7)☒ Claim(s) *52,56-58,63 and 64* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

File

DETAILED ACTION

Please note that the Examiner of record and art unit has changed. The Examiner of record is now **Joseph T. Woitach** and the group art unit is now **1632**.

This application claims benefit to provisional applications 60/127,452, filed April 1, 1999, and 60/173,826, filed December 30, 1999.

Applicants' amendment filed January 23, 2002, paper number 13 has been received and entered. Claims 7-17, 29, 31-41 and 43-45 have been canceled. Claims 46-65 have been added. Claims 1-6, 18-28, 30, and 46-65 are pending. Claims 1-6, 18-28 and 30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10. Claims 46-65 are currently under examination.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Objections

Claims 46, 48, 52, 53, 60 and 61 are objected to because of the following informalities:

The claims recite and are drawn to a non-elected invention. Applicants have elected examination of the human PAMP (see paper number 10), however the claims still recite PAMP from other organisms. Appropriate correction is required.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e).

Applicants point out that SEQ ID NO: 2 of the priority application comprises the instantly claimed SEQ ID NO 14 with the addition of 23 amino acid residues. Further, SEQ ID NO: 1 of the priority document contains <u>almost</u> the entire coding sequence for PAMP. Applicants argue that one of skill in the art using the teachings of the priority document could have deduced the instantly claimed sequences. Further, it is argued that one of skill in the art could have identified the specific mutations described in the present disclosure. See Applicants amendment, pages 7-8. Applicants arguments have been fully considered. but not found persuasive.

As noted in the previous office action, the disclosure of the invention in the parent application and in the continuing application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *In re Ahlbrecht*, 168 USPQ 293 (CCPA 1971). In the instant case, Examiner agrees that one of skill in the art using the information provided in the

priority documents could have performed further experiments to determine the specific sequences instantly disclosed, however the ability to isolate a sequence does not meet adequate written description under 35 USC 112, first paragraph (Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991)). If one were to accept Applicants then any sequence which is capable of binding PAMP could be used to derive the specific PAMP sequences and derive mutants thereof. This argument is not found persuasive because it would not provide the necessary detail on the sequence, wherein one could distinguish the resulting sequence as PAMP or as a mutant PAMP.

Therefore, it is maintained that there is not adequate support in provisional application 60/127,452 for the nucleic acid of SEQ ID NO:13, the amino acid sequence of SEQ ID NO:14, or for methods or compositions comprising nucleic acids encoding the mutant PAMP proteins recited in claim 14.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 51, 54, 55, 59-62 and 65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants argue that the present specification discloses PAMP from four different species of organisms, and thus, provides PAMP structure. It is pointed out that PAMP is characterized by its ability to bind presenilins, and thus, a functional feature of PAMP is described. See Applicants' amendment, page 11. Applicants' arguments have been fully considered, but not found persuasive.

Examiner notes that specific PAMP sequences from four organisms are disclosed and that based on sequence homology, they may interact with presenilin. However, the specification defines the term "PAMP" a functionally active fragments. It is proposed that the function of PAMP is associated with various pathways, however the present disclosure clearly states that the exact role of PAMP is not defined (page 42, lines 9-11). Lacking any function for PAMP, one could not determine if a sequence derived from another protein would be considered a PAMP. Alternatively, a sequence which interacts with presenilins would not necessarily be considered a PAMP, for example an antibody. Further, while the sequences from four organisms are disclosed, there is very low homology among the species, and no description besides the sequences which point to critical amino acids or elements of domains which uniquely defines a protein sequence as a PAMP (see for example figure 1). The claimed invention as a whole is not

adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998). In the instant case, Applicants have cloned and defined several unique nucleic acid sequences, however the specification fails to describe the relevant identifying characteristics of all the nucleic acid sequences, or of the encoded proteins which uniquely define the sequences as a PAMP. The method used to isolate the disclosed sequences is not presented in detail, and based on the very low homology among the disclosed sequences, the skilled artisan cannot envision all the other possible variant nucleic acid sequences from all the other species that exist in nature, nor if the sequence would be considered wild type or mutant, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack

of written description for that broad class. The specification provided only the bovine sequence. In the instant case, the disclosure of four specific sequences lacking significant homology is not adequate to provide written description for any other PAMP that may exist in nature. Further, it does not provide the necessary guidance to determine if the sequence is wild type or mutant, nor does it provide guidance to active fragments which is encompassed by the term PAMP.

Claims 51, 54, 55, 59-62 and 65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids comprising a PAMP-encoding nucleic acid of SEQ ID NO:13 or nucleic acids encoding the amino acid sequence of SEQ ID NO:14, does not reasonably provide enablement for any and all PAMP functional fragments or mutant PAMP-encoding nucleic acids .

Applicants argue that the present specification provides guidance on how to isolate and characterize PAMP sequences from various species, and that mutations can be introduced by standard techniques. applicants pont to pages 9-10 of the present specification for support of particular domains and motifs in human PAMP, and argue that by comparing the sequences of other species one could further define information on the structure of PAMP. Finally, Applicants point to the biochemical clues for the potential role of PAMP in Alzheimer's and more specifically as a protein that interacts with PS1, PS2 and β-APP, and argue that this involvement implicates specific features of PAMP. See Applicants' amendment, pages 12-13. Applicants' arguments have been fully considered, but not found persuasive.

As noted in the previous office action the specification teaches that "PAMP" refers to "functionally active fragments of the protein", including peptides that contain a PAMP epitope or "a conserved domain relative to the *D. melanogaster* and *C. elegans* orthologues" (page 10, lines 11-26). Further, the art teaches that an immunogenic portion can be only 5 amino acids in length (Levinson *et al.*). Examiner agrees that there appears to be a correlation with PAMP and neurological disorders, and that orthologues of PAMP are present in several species but as indicated in Applicants' arguments and supported by the present specification, the specific function of PAMP is unknown. Further, Examiner agrees that the potential roles for deduced motifs and domains can be further defined given the general level of skill in the art. However, given the relatively uncharacterized nature of this protein and the broad scope of subject matter embraced by the above definition of PAMP, the specification fails to provide adequate guidance for making and using PAMP- or mutant PAMP-encoding nucleic acids commensurate with the broad scope of the claims subject matter. Further, while one of skill in the art could perform further experiments to determine which of the proposed motifs are functionally important, the specification fails to provide adequate guidance on how to use each of these different and separate isolated domains of PAMP commensurate with the above definition, particularly since it fails to provide adequate guidance concerning their specific structure/function relationship. Even if one were to concede that disclosure of the four sequences provides a basis for comparison and identification of similar sequences, the conserved domains represent nothing more than a starting point for further experimentation. Finally, the term "mutant PAMP" broadly embraces virtually

any nucleotide sequence encoding a PAMP that is different from wild-type. In the absence of any specific functional limitation associated with a mutant, the recitation of the term "mutant PAMP" encompasses all PAMP variants which may or may not have desirable or useful function. Without the necessary guidance, the specification fails to provide a sufficiently enabling disclosure for making and using any and all PAMP functional fragments or mutant PAMPs commensurate with the scope of the claimed subject matter.

Thus, in view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required undue experimentation to make and/or use the invention as claimed, and therefore, the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 51, 54, 55, 59-62 and 65 are rejected under 35 U.S.C. 102(b) as being anticipated by Genbank Accession Number D87442.

Applicants point out that D87442 differs from the instantly disclosed sequences by the first methionine amino acid residue, and argue that the disclosure of this sequence does not teach

the PAMP protein. See Applicants' amendment, page 14. Applicants' arguments have been fully considered, but not found persuasive.

Examiner notes that for anticipation a reference must teach each and every aspect of the claimed invention (MPEP 706.02). In the instant case, the claims are being interpreted to encompass a PAMP as defined in the present disclosure which encompasses wild type, allelic variants, and mutant forms of PAMP. As noted in the previous office action, Genbank Accession Number D87442 discloses a nucleic acid encoding a functional fragment of a presenilin associated membrane protein (PAMP) whose nucleic acid sequence is 99.9% identical to positions 145-2949 of SEQ ID NO:13, differing from the nucleic acid encoding a PAMP of SEQ ID NO:13 only insofar as missing the first two nucleotides of the initiation codon (i.e. AT) and containing two degenerate nucleotide positions corresponding to nucleotides 2274 and 2281 of SEQ ID NO:13. Given that the first methionine of the putative signal peptide sequence of the encoded PAMP protein is not present the PAMP product present in the membrane (the signal sequence is cleaved away from the processed membrane form), the nucleic acid sequence of Genbank Accession Number D87442 reads on an isolated nucleic acid encoding a functional PAMP fragment. Further, since the prior art sequence is not 100% identical (lacks first methionine) to SEQ ID NO:13, it would be broadly interpreted as reading on a mutant PAMP. The courts have stated that because the office does not have the facilities for examining and comparing applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional

characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See *Ex parte Phillips*, 28 USPQ 1302, 1303 (BPAI 1993), *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ2d 1922, 1923 (BPAI 1989). In the instant case, because the polynucleotide disclosed in D87442 meets the physical limitations of the broad definition encompassed by PAMP as defined in the present specification, the sequences disclosed anticipate the sequences intantly claimed.

Conclusion

Claims 46-50 are allowed. Claims 52, 53, 56-58, 63 and 64 are objected to because they depend on rejected claims, however would be allowable if rewritten as independent claims encompassing all the embodiments of the independent claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist Pauline Farrier whose telephone number is (703)305-3550.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1800 7630